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LATENT PNEUMOCOCCEMIA.*

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ALTHOUGH much work has been done on pneumococcal infections and pneumococcemia our knowledge of the mechanism of these processes is still in its infancy. It is only within recent years that it has been established by Fraenkel,[1] Prochaska,[2] and others, but especially Rosenow,[3] that in every case of pneumococcal pneumonia we have a pneumococcemia. Heretofore pneumococcemia was believed to occur practically only in fatal cases, and accordingly the entrance of the pneumococcus into the general circulation was viewed with grave apprehension. With the establishment of this pneumococcemia the question naturally arises, is this general invasion primary and the pulmonary process secondary, simply a localization at the *locus minoris resistentiae;* or is the reverse true and the breaking through into the blood stream but a natural consequence of the local involvement. Experimentally Washburn,[4] Fraenkel and Schultz[5] were able to produce pulmonary conditions identical with those found in man by means of intravenous and intraperitoneal injections, and inclined to the former view. Rosenow was able to verify their results and, moreover, succeeded in demonstrating the pneumococcus in the blood in five cases before any local physical signs were present.

Intimately associated with this problem is the question, What is the fate of the pneumococci in the blood, especially with relation to crisis? Clinically the pneumococcal joint localizations, usually postcritical, as pointed out by Herrick,[6] clearly show that the pneumococcus can persist in the blood after crisis. Its virulence in this case is indicated by the fact that it does produce pathological processes. The

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[1] *Deutsche med. Wchnschr.*, 1901, 27, p. 298.

[2] *Deut. Arch. f. klin. Med.*, 1901, 70, p. 559; *Centralbl. f. inn. Med.*, 1900, 21, p. 1145.

[3] *Jour. Infect. Dis.*, 1904, 1, p. 280. [4] *Lancet*, 1902, 163, p. 301.

[5] *N. Arch. d. Sci. biol. d. St. Petersburg*, 1901 8, p. 1.

[6] *Am. Jour. Med. Sc.*, 1902, 124, p. 1234.

same may be said of pneumococcal endocarditis and many other postcritical metapneumonic processes.

We have but few isolated facts at hand bearing on this intricate problem. Baudel[1] in 1899 obtained the pneumococcus from the blood as late as 25 days after crisis. Prochaska demonstrated the pneumococcus in the blood four times after crisis; on the day after crisis in one uncomplicated case, and in one complicated by serous pleuritis; two days after crisis in a case complicated by muscle abscess; three days after crisis in a case of delayed resolution. Rosenow in his series of 145 cases, examined eight cases from 4 to 36 hours after crisis, finding the pneumococcus four times, i. e., in 50 per cent; more recently three unpublished cases within 24 hours after crisis. Recently Tizzoni and Panichi[2] found the organism in five cases, 30, 31, 31, and 56 days, respectively, after crisis and over 15 months after convalescence. They also demonstrated pneumococci in "hypervaccinated" rabbits 11 months after injection.

During the past winter I have made careful observations in regard to this question on 21 cases of lobar pneumonia chosen at random. Blood cultures were made in broth and milk. In all the cases one or more cultures were made before crisis and usually several cultures were made on successive days after crisis.

The pneumococcus was recovered after crisis in six of the 21 cases of lobar pneumonia. It was not obtained before crisis in five of the remaining 15 cases, and therefore these should be set aside as not comparable. Thus the pneumococcus was isolated after crisis in six out 16 cases, or in 37 per cent of the cases showing the organism before crisis.

BRIEF STATEMENT OF CASES.

1. Age 15 months. Typical left lobar pneumonia. Pneumococci in the blood. Crisis five days after admission to the hospital. Culture from the blood eight days after the temperature had become normal gave pneumococci.

2. Male, age 40, alcoholic. Typical left upper lobe pneumonia. Crisis occurred on same day, but three days later the temperature became variable (96.8°–100°) with persistent leucocytosis. Fifteen days later had a chill with a rise of temperature, returning to normal the next day. Patient had a chill on three successive days, the

[1] *Rif. Med.*, 1899, 11, p. 170.

[2] *R. Accad. d. Sc. di Bologna*, 1905, jan. 15; *Rendiconti Accad. dei Lincei*, XIV, 2, sèrie, 16 juillet, 1 905, pp. 107–14; 6 aout, 1906 (Abst. *Bull. de l'Inst. Pasteur*, 1905 3 p. 420); *Centrabl. f. Bakt.*, 1905 36, pp. 25–47.

temperature returning to and remaining normal 20 days after the original crisis. A blood culture secured during the second chill (17 days after the crisis) yielded abundant growth of pneumococci. Delayed resolution present.

3. Colored, age 34, cook. Typical left lower lobe pneumonia. Temperature remained high for 11 days after admission, then became irregular for six days when it became normal. Positive cultures were obtained four days after admission and again two days after his temperature had become normal. Delayed resolution present.

4. Male, age 24, colored. Typical left lower lobe pneumonia. Crisis occurred eight days after admission, but two days later temperature again rose and remained irregular (97.4°-103°), until the 15th day after crisis. Signs of delayed resolution present. Cultures before crisis and 16 days after crisis gave positive results.

5. Male, age 31, laborer. Typical left lower lobe pneumonia with extension to left upper lobe seven days after admission. Crisis 10 days after admission. Blood cultures before crisis and eight hours after crisis were positive.

6. Male, age 39, machinist, ward man in the hospital. Taken suddenly with right lower lobe pneumonia. Blood cultures three hours after chill sterile, but cultures taken 24 hours after chill and again eight hours after crisis, which occurred on the third day, gave pneumococci.

We see that the pneumococcus was found six times after what appeared to be a typical crisis; three times eight hours after, and in three cases complicated by delayed resolution 7, 16, and 17 days after crises, respectively, and one to two days after temperature finally remained normal. No attempt was made to ascertain how long after crisis the organisms could be obtained.

CHARACTERISTICS OF ORGANISMS OBTAINED FROM THE BLOOD AFTER CRISIS.

Tizzoni and Panichi claim that the organisms they isolated after crisis were non-virulent and atypical morphologically, resuming, however, typical appearances after a short period of cultivation. These organisms, they assume, had been changed, maintaining an inoffensive existence in the blood. I have not been able to reach the same conclusions from the study of the organisms obtained by me after crisis.

Morphology.—The organisms obtained in all cases were typical lance-shaped, encapsulated pneumococci, grouped usually in pairs. All fermented inulin and also formed the characteristic green zone about the colonies on blood agar.

Virulence.—Four strains were tested for virulence by intraperitoneal injection of 24-hour broth cultures of rabbits with the following results:

TABLE 1.

	Case	Dose	Time of Death
Rabbits, weight 2,000 to 2,500 grams.....	1	3–5 c.c.	24–36 hours
" " 1,700 to 1,900 "	2	4–5	24 "
" " 1,700 "	5	4	36 "
" " 1,300 "	6	5	48 "

We see that all the organisms tested show considerable virulence for rabbits, giving results similar to those obtained with organisms isolated from the same patients before crisis.

Relation of the organisms to phagocytosis.—Metchnikoff in his early studies of phagocytosis made the important observation that virulent streptococci were not susceptible to phagocytosis. More recently the same results have been obtained with virulent pneumococci. Moreover, it has been found by Rosenow that this resistance to phagocytosis as well as the virulence is readily lost by artificial cultivation under favorable conditions, but can be again restored, although with difficulty, by repeated passages through animals. Because of this intimate association of virulence and resistance to phagocytosis, it would seem reasonable to expect that the organisms considered in the foregoing would be relatively insusceptible to phagocytosis. Hence the experiments whose results are given in Table 2 were made.

TABLE 2.

ABSENCE OF PHAGOCYTOSIS OF ORGANISM FROM CASE 1.

PNEUMOCOCCAL SUSPENSION+ BLOOD OR SERUM+WASHED BLOOD CORPUSCLES	PHAGOCYTOSIS (20 LEUCOCYTES COUNTED AT END OF ONE HOUR	
	Pneumococcus Case 1 (Isolated after Crisis)	Avirulent Pneumococci
Human blood (defibrinated).....	0	25+
Human serum 0.25+guinea-pig leucocytes 0.25.....	0	25+
Guinea-pig exudate (whole) 0.5.....	0	25+
Dog blood (defibrinated) 0.5	0	23
Dog serum 0.25+washed human corpuscles 0.25	0	25+

The above table shows that the stain isolated from Case 1 after crisis is not susceptible to phagocytosis by the leucocytes in normal human blood, dog blood, or guinea-pig exudate, or by guinea-pig leucocytes in human serum or human leucocytes in dog serum. As normal sera were used in the above experiments, it might be objected

that even though these organisms were not sensitized by normal serum they readily become susceptible to phagocytosis when treated with the serum of the patient harboring the organisms. With this in view the following experiment was made, the result showing that the pneumococcal strains were not taken up by the phagocytes in normal blood nor in the blood from the patients from whom the organisms were isolated.

TABLE 3.

ABSENCE OF PHAGOCYTOSIS OF PNEUMOCOCCI IN BLOOD FROM PATIENTS, FROM WHOM THEY WERE OBTAINED.

Blood+Pneumococcal Suspension	Phagocytosis (20 Leucocytes Counted after 1 Hour)
Blood Case 2 after crisis+pneumococcus Case 2 isolated after crisis	0
Blood Case 2 after crisis+nonvirulent pneumococcus[1]	21
Blood Case 5 before crisis+pneumococcus Case 5 isolated before crisis	0
Blood Case 5 before crisis+nonvirulent pneumococcus	7
Blood Case 5 after crisis+pneumococcus Case 5 isolated before crisis	0
Blood Case 5 after crisis+nonvirulent pneumococcus	23.4
Blood Case 5 after crisis+pneumococcus Case 5 isolated after crisis	0
Blood Case 6 after crisis+pneumococcus Case 6 isolated after crisis	0
Blood Case 6 after crisis+nonvirulent pneumococcus	11

SUMMARY AND CONCLUSIONS.

The above results show that the pneumococcus does exist in the blood of a large per cent of the pneumonia patients after crisis. This is in accord with the findings of other observers. How long they do remain is as yet undetermined, perhaps a few hours or a few days in cases running a normal course to several weeks in cases complicated by delayed resolution, endocarditis, or some other metapneumonic process. Whether they can exist in the blood of uncomplicated cases for weeks or even years as Panichi states is, to say the least, highly questionable. Pneumococci isolated after crisis are virulent for rabbits to the same degree as are the precritical organisms derived from the same patients. Virulence is also indicated by the fact that a pneumococcic strain is insusceptible to phagocytosis by normal human and dog blood and guinea-pig exudate; furthermore, by the facts that other strains show no evidence of phagocytosis when treated with normal blood nor with blood drawn from the homologous patient after crisis, when we would expect the opsonic index to be at its highest.

We are therefore forced to conclude that crisis cannot be identical with a sudden disappearance of all organisms from the blood of a

pneumonia patient. It would be more reasonable to assume that crisis marked the point where the increase is more than counterbalanced by the destruction of the organism, presumably by phagocytes. (Further reference will be made to this point in another paper.) Neither do the experimental results nor the clinical evidence appear to me to permit us to assume that the pneumococci at the time of crisis acquire some mysterious properties which render them nonvirulent and harmless and yet insusceptible to phagocytosis.

In view of the fact that during the course of pneumonia a number of metabolic products are more readily formed (acids, ferments, and the like), locally as well as in the blood, the chemistry of which is wholly unknown, it would seem better not to connect the phenomenon of crisis too closely with the presence of the pneumococcus in the blood.

I herewith wish to express my thanks to the Rush Alumni Association for making the work possible; to Dr. Hektoen, under whose direction it was done; and to the house staff of the Cook County Hospital for the many courtesies shown.